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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/905,657	07/13/2001	Christa Lechelt-Kunze	Mo-6431/LcA 34,730	5977

34469 7590 05/20/2003

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EXAMINER

SAIDHA, TEKCHAND

ART UNIT

PAPER NUMBER

1652

DATE MAILED: 05/20/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/905657

Applicant(s)

Lechelt-Kunze et al

Examiner

T. Saidha

Group Art Unit

1652

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—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

- ☒ Responsive to communication(s) filed on 12/2/02
- ☐ This action is **FINAL**.
- ☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

- ☒ Claim(s) 15-17, 20-21, 23-46 is/are pending in the application.
- Of the above claim(s) 17, 20-21, 23-26 & 31-36 is/are withdrawn from consideration.
- ☐ Claim(s) _____ is/are allowed.
- ☒ Claim(s) 15-16, 27-30 & 37-46 is/are rejected.
- ☐ Claim(s) _____ is/are objected to.
- ☐ Claim(s) _____ are subject to restriction or election requirement.

Application Papers

- ☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.
- ☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.
- ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.
- ☐ The specification is objected to by the Examiner.
- ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119 (a)-(d)

- ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).
- ☒ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been received.
- ☐ received in Application No. (Series Code/Serial Number) _____.
- ☐ received in this national stage application from the International Bureau (PCT Rule 1.7.2(a)).

*Certified copies not received: _____

Attachment(s)

- ☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____ ☐ Interview Summary, PTO-413
- ☒ Notice of Reference(s) Cited, PTO-892 ☐ Notice of Informal Patent Application, PTO-152
- ☐ Notice of Draftsperson's Patent Drawing Review, PTO-948 ☐ Other _____

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DETAILED ACTION

1. The Group and/or Art Unit location of your application in the PTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1652.

2 ***Election***

Applicant's election of group I (claims 15-16, 27-30 & 37-46) in Paper No. (filed 12.02.02) is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 17, 20-21, 23-26 & 31-36 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

3. ***Priority***

Acknowledgment is made of applicants' claim for priority based on an application filed in Germany on 07/18/2000.

4. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

5. Claims 15-16, 27-30 & 37-46 are under consideration in this examination.

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6. ***Claim Rejections - 35 U.S.C. § 112 (first paragraph)***

Enablement

Claims 15-16, 27-30 & 37, 39-40 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited to a method of determining a binding or inhibitor or activator chemical compound using the polypeptide of SEQ ID NO : 2 or a polypeptide encoded by the DNA of SEQ ID NO : 1, does not reasonably provide enablement for any biologically active and a very long chain fatty acid elongase (VLCFAE) which could be any of the four enzymes of the 'fatty acid elongase complex' described in U.S.P. 6,307,128 (see column 1, line 50 through column 2, line 41); and where each of the enzyme having 60% identity to SEQ ID NO: 2. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

The claims are directed to a method of determining a binding or inhibitor or activator chemical compound using the polypeptide of SEQ ID NO : 2 using (a) any of the 4 enzyme belonging to the elongase enzyme complex [U.S.P. 6,307,128 (see column 1, line 50 through column 2, line 41)] or (b) where SEQ ID NO : 2 is modified by substitution, insertion or addition or deletion to result in a polypeptide which is 60% identical and yet biological active. However, the guidance provided for is minimal and lends support to only in the isolation of a single polypeptide sequence of SEQ ID NO : 2 (or the encoding DNA of SEQ ID NO : 1) with no assays procedures to test for (a) elongase enzyme or biological activity, [Is there an elongase assay ?], (b) binding assays (c)

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inhibitor assay or compounds used or (d) activator assay or chemical compound(s) used in the assay, which guidance is inadequate for one skilled in the art to develop a method claimed.

Factors to be considered in determining whether undue experimentation is required, are summarized in *re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988) [*Ex parte* Forman [230 USPQ 546 (Bd. Pat. App. & Int. 1986)]]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim. The factors most relevant to this rejection are the scope of the claims, unpredictability in the art, the amount of direction or guidance presented, and the amount of experimentation necessary.

Claims 15-16, 27-30 & 37, 39-40 are so broad as to encompass a method of identifying an inhibitor or binding or activator compound of any elongase from any species, which as defined in the above cited U.S.P. '307 further comprises of or is a complex of four enzymes (claims 15-16), or having 60% identity to SEQ ID NO: 2 (claims 27-30 & 37, 39-40). The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of elongases broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of

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modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the nucleotide and encoded amino acid sequence of elongase of SEQ ID NO : 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass all modifications of any elongase with 60% identity to the enzymes of SEQ ID NOS: 2, because the specification does not establish: (A) regions of the protein structure which may be modified without effecting elongase activity; (B) the general tolerance of elongase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any elongase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the

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claims broadly including elongase with an enormous number of amino acid modifications of the of SEQ ID NOS: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of elongase having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue in using the modified enzyme in the method claimed. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

7. ***35 U.S.C. § 112, first paragraph (Written Description)***

Claims 15-16 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Claims 15-16 are directed to a method of determining a chemical compound which binds to or inhibits or activates a polypeptide with the biological activity of a very long chain fatty acid elongase (VLCFAE).

Claims 15-16 do not provide any structural information. The specification, however, only provides a single representative species from *Arabidopsis* polypeptide of SEQ ID NO : 2 (or the encoding DNA of SEQ ID NO : 1). There is no disclosure of any particular structure to function/activity relationship in the single disclosed species to other species where such sequences are conserved in order to establish a relationship among species to have elongase activity. The

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specification also fails to describe additional representative species of these elongases, or chemical compounds to be contacted to the elongases by any identifying structural characteristics other than the properties or activity recited in claims, for which no predictability of structure is apparent. Given this lack of additional representative species, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Therefore, the written description requirement is not satisfied.

8. ***Claim Rejections - 35 U.S.C. § 112*** (second paragraph)

Claim 15 is rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 15, line 1, recites inhibitors and/or activators, which is indefinite because 'inhibitor and activator are not alternate expressions. It is suggested to separate the claims using the two expressions.

Claims 27-30 & 41-44 are included in the rejection for failing to correct the defect present in the base claim(s).

9. Claims 45-46 are objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s)

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in independent form. Claim 45 depends from claim 17, a non-elected claim. Correcting the dependency will overcome this objection.

Claim 46 is included in the objection for failing to correct the defect present in the base claim(s).

10. ***Claim Rejections - 35 U.S.C. § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 15-16, 27-30 & 37-40 are rejected under 35 U.S.C. 102(e) as being anticipated by Jorwarski et al. (U.S.P. 6,306,128). Jorwarski et al. (U.S.P. 6,306,128) teach nucleic acid encoding fatty acid β -keto acyl synthase for producing VLCFA (an elongase). The prior art (U.S.P. 6,306,128) sequence of SEQ ID NO : 8 is from *Arabidopsis*. Applicants SEQ ID NO : 2 is 99.8% identical to the disclosed Sequence of SEQ ID NO : 8. The patent further teaches altering the levels of long chain fatty acid (VLCFA) by differential nucleotide expression. The patent also teaches a method of evaluating chemical inhibitors such as, cerulenin, on β -keto acyl synthase (**KAS**) activity (see tables 7-9 & columns 17-18) and inhibitors are known to form a tight binding complex with

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elongase, the binding properties of the compounds can also be evaluated. All the claim limitations being taught, the reference anticipates the claims.

11. ***Claim Rejections - 35 U.S.C. § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 41-46 are rejected under 35 U.S.C. 103(a) as being unpatentable over U.S.P. 6,306,128 *and* Accession No. O64846.

Jorwarski et al. (U.S.P. 6,306,128) teach nucleic acid encoding fatty acid β -keto acyl synthase for producing VLCFA (an elongase). The prior art (U.S.P. 6,306,128) sequence of SEQ ID NO : 8 is from *Arabidopsis*. Applicants SEQ ID NO : 2 is 99.8% identical to the disclosed Sequence of SEQ ID NO : 8. The patent further teaches altering the levels of long chain fatty acid (VLCFA) by differential nucleotide expression. A method for evaluating chemical inhibitors such as, cerulenin, on β -keto acyl synthase (**KAS**) activity (see tables 7-9 & columns 17-18) is taught by the reference. The patent does not teach the protein sequence which is 100% identical to Applicants SEQ ID NO : 2.

Accession No. O64846 is a KAS protein (Fiddlehead protein) and is 100% identical to Applicants' SEQ ID NO : 2.

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From the teachings of the art presented here, and summarizing the similarities of the prior art in comparison to the claimed invention, the references teach all the claim limitations including the ones which are obvious and therefore not stated in the rejection.

Thus from the knowledge available in the teachings of the prior art, it would have been obvious to one having ordinary skill in the art at the time the invention was made to use the existing method of Jorwarski et al. for testing old or new chemical compounds as probable candidates for an inhibitor or activator or one that will bind to the enzyme which may be an inhibitor, by substituting accession no. O64846 with the sequence of Jorwarski et al. having known KAS activity in order to screen for other inhibitor compounds or compounds that bind, to develop a method to better regulate *Arabidopsis KAS protein* or mutants by altering the VLCFA by chemical means and do so with a reasonable expectation of success. One of ordinary skill in the art would have been motivated in view of the fact that VLCFA are not desirable in edible oil (see U.S.P. - column 1, lines 14-30) and a suitable inhibitor or a binding compounds will be able to alter the ratio of fatty acids in the plant product and thus control quality.

Thus, the claimed invention was within the ordinary skill in the art to make and use at the time was made and was as a whole, *prima facie* obvious.

12. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tekchand Saidha (Ph.D.) whose telephone number is (703) 305-6595. The examiner can normally be reached on Monday-Friday from 8:15 am to 4:45 pm.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy, can be reached at (703) 308-3804. The fax phone number for this Group in the Technology Center is (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.



Tekchand Saidha
Primary Examiner, Art Unit 1652
May 15, 2003